

REMARKS

Claims 59, 61-65, 67-76, and 78-82 and 84-101 are pending in the instant application. Reconsideration of the claims in light of the amendments and remarks that follow is respectfully requested.

Examiner Interview Summary

On September 8, 2003, Richard Trecartin and Steven Lendaris (attorneys for the applicant) discussed the pending rejections with Examiner Marschel. Examiner Marschel preliminarily indicated that the claims 59, 61-65, 67-76,

The Amended Claims

The pending claims, as currently amended, include new Claims 92-101. These claims were not discussed during the Examiner Interview on September 8, 2003, however these claims depend from Claim 91, which was discussed, and are similar to other dependent claims pending in the case.

35 U.S.C. § 112, second paragraph

Claims 59, 61-65, 67-69, and 81-90 stand rejected under 35 U.S.C. § 112, second paragraph, as being vague and indefinite. In particular, the Examiner has rejected Claim 81, and all claims depending from Claim 81, as unclear in that the preamble states that the claim is a method of subjecting a sample to rapid thermal cycling to amplify a nucleic acid, but steps a) and b) do not refer to amplification or nucleic acids. As Claim 81, as presently amended, now refers to amplification of nucleic acids, withdrawal of this rejection is respectfully requested.

Claim 81, and all claims depending therefrom, also stand rejected as vague and indefinite in that the preamble states that the claim involves subjecting a sample to rapid thermal cycling, but steps a) and b) do not refer to such cycling. As Claim 81, as presently amended, now refers to cycling, i.e. by repeating steps a) through c) at least one time, withdrawal of this rejection is respectfully requested.

Claim 59, and all claims depending therefrom, stand rejected as vague and indefinite in that the preamble states that the claim involves subjecting a sample to rapid thermal cycling, but steps a) and b) do not refer to such cycling. As Claim 59, as presently amended, now refers to cycling, withdrawal of this rejection is respectfully requested.

Claim 83 stands rejected as lacking clear antecedent basis for the phrase, "the steps." As Claim 83 is canceled by this amendment, withdrawal of this rejection is respectfully requested.

Claim 90 stands rejected as lacking clear antecedent basis for the phrase, "the amplification products" in line 2. As Claim 90, as presently amended, now provides clear antecedent basis for the phrase, "the amplification products," withdrawal of this rejection is respectfully requested.

35 U.S.C. § 102(e)(2)

Claims 81, 83 and 84 stand rejected under 35 U.S.C. § 102(e)(2) as being anticipated by Mullis *et al.* (U.S. Patent No. 5,656,493, "Mullis *et al.*"). In particular, the Examiner asserts that Mullis *et al.* teach a general scheme for thermally cycling a sample. Additionally, at page 8 of the Office Action mailed April 4, 2003, the Examiner concedes that each cycle in Mullis *et al.* is completed in no less than about 120 seconds.

Claim 81 of the instant invention is directed to a method of subjecting a sample to rapid thermal cycling in order to amplify a nucleic acid. The method involves raising the temperature of a sample to a first temperature and holding the sample at that temperature for a period of time, followed by lowering the temperature of the sample to a second temperature at a rate at least about 1.5 °C per second and holding the sample at that second temperature for a second period of time. In addition, Claim 81, as currently amended, recites that these steps are repeated at least once and the entire cycle is completed within about 30 second to 60 seconds.

For an anticipation rejection under 35 U.S.C. §102 to be proper, a single reference must expressly or inherently disclose each and every element of a claim. *In re Paulsen*, 31 USPQ2d 1671, 1673 (Fed. Cir. 1994); MPEP § 2131 (citing *Richardson v. Suzuki Motor Co.*, 9 USPQ2d

1913, 1920 (Fed. Cir. 1989). As discussed above, Claim 81 of the instant application relates to a method of subjecting a sample to rapid thermal cycling, wherein each cycle is completed in no more than 60 seconds. As is also discussed above, the Examiner conceded that Mullis *et al.* teach cycling times of no less than about 120 seconds. Accordingly, Mullis *et al.* does meet each and every element of the instant claims and withdrawal of this rejection is respectfully requested.

35 U.S.C. § 103(a)

Claims 59-62, 64-65, 67-68, 70-72, 74-76, 78-79, 81, 83-86, and 88 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Mullis *et al.* In particular, the Examiner points to various descriptions in the reference of time periods and temperature ranges over which thermal cycling can be practiced. For example, the Examiner argues that using the minimum time periods disclosed in Mullis *et al.* for temperature rise, fall, denaturation and enzyme polymerization, that the minimum time for a single cycle is 120 seconds. Using this minimum 120 second cycle time, the Examiner then argues that it is "functionally" equivalent to the instant invention and thus renders the instant invention obvious.

When rejecting a claim under 35 U.S.C. § 103, the Examiner bears the burden of establishing a *prima facie* case of obviousness. *In re Bell*, 26 USPQ2d 1529 (Fed. Cir. 1993). To establish a *prima facie* case the Examiner must show that the prior art reference, or references when combined, teach or suggest each and every limitation of the claimed invention. M.P.E.P. § 706.02(j).

As discussed above, the Examiner has functionally equated the 120 second cycle time with the maximum 60 second cycle time of the instant invention. However, Applicants respectfully point to Figure 9A to illustrate that such differences in cycle time are not functionally equivalent. The results of PCR reactions A-D in Figure 9A demonstrate that cycling times of longer than 120 seconds (reactions A and B in the Figure) clearly generate far more spurious amplification products than those with cycling times of less than 120 seconds (reactions C and D in the Figure). Furthermore, the claims, as currently amended, are directed to cycle times from "about 30 seconds up to 60 seconds" and thus no longer contain the "about 60 seconds" language used by the Examiner in equating the instant invention to the 120 second

cycles disclosed in Mullis *et al.* In light of these facts, Mullis *et al.* fails to teach or suggest cycle times of about 30 seconds to up to 60 seconds and therefore the Examiner has failed to establish a prima facie case of obviousness. Accordingly, withdrawal of this rejection is respectfully requested.

Claims 59-62, 64-65, 67-68, 70-72, 74-76, 78-79, 81, 83-86, 88, and 90 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Mullis *et al.*, in view of Ward *et al.* Mullis *et al.* is discussed above. Ward *et al.* is cited by the Examiner to provide teaching related to fluorescence-mediated detection of amplification products.

The standard for establishing a prima facie case of obviousness is stated above.

As is also described above, Mullis *et al.* does not teach or suggest the claims as presently amended. Although Ward *et al.* teaches a variety of labeled compounds, including fluorescently labeled nucleotides, it makes no mention of thermal cycling nucleic acids and therefore, cannot correct for the deficiency of Mullis *et al.* Accordingly, the Examiner has failed to establish a prima facie case of obviousness and withdrawal of the rejection is respectfully requested.

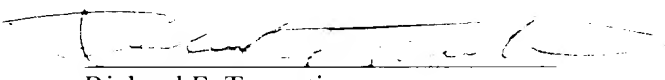
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CONCLUSION

On the basis of the amendments and remarks presented herein, Applicants believe that this application is now in condition for immediate allowance. Applicants respectfully request that the Examiner pass this application to issue, and early notice of such is requested. This paper is filed under 37 C.F.R. section 1.34(a).

Respectfully submitted,
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